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=> untranslated or utr

L1        39186 UNTRANSLATED OR UTR

=> nucleic acid

L2       326505 NUCLEIC ACID

=> ?nucleotide

L3       741097 ?NUCLEOTIDE

=> l2 or l3

L4       992685 L2 OR L3

=> l1 and l4

L5        20263 L1 AND L4

=> endoplasmic reticulum

L6       107392 ENDOPLASMIC RETICULUM

=> l5 and l6

L7           94 L5 AND L6

=> l7 and secret?

L8           16 L7 AND SECRET?

=> l8 and 1970-2000/py

   2 FILES SEARCHED...
L9           13 L8 AND 1970-2000/PY

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PROCESSING COMPLETED FOR L9
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L10 8 DUP REM L9 (5 DUPLICATES REMOVED)

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L10 ANSWER 1 OF 8 CAPLUS COPYRIGHT 2002 ACS
TI Methods and means for expression of mammalian polypeptides in monocotyledonous plants
AB Rice, wheat, and other monocotyledonous plants are transformed with expression cassettes for prodn. of mammalian polypeptides, such as antibodies. **Endoplasmic reticulum** (ER) retention signals, 5'-**untranslated** regions, and leader peptides are employed in various combinations to provide high expression yield. Multi-chain complexes such as four-chain **secretory** antibodies are produced by expression of component polypeptides from sep. vectors all introduced into the same cell by transformation.
SO PCT Int. Appl., 77 pp.
CODEN: PIXXD2

L10 ANSWER 2 OF 8 CAPLUS COPYRIGHT 2002 ACS
TI Erythropoietin mutants with altered biological activity
AB The invention relates to DNA encoding modified, **secretable** erythropoietin proteins whose ability to regulate the growth and differentiation of red blood cell progenitors are different from the wild-type recombinant erythropoietin. The invention also relates to methods of modifying or altering the regulating activity of the **secretable** erythropoietin proteins and the use of the modified **secretable** erythropoietin proteins, for example, in in vivo therapeutics. Thus, **oligonucleotide**-directed mutagenesis was used to create mutant erythropoietin which resulted in substitution of amino acids at positions 100-109 within Domain 1. Arginine-103 was crit. for erythropoietin's biol. activity, and serine-104, leucine-105, and leucine-108 appear to play a role, as indicated by the decreased biol. activity of these mutants. Some of the mutant erythropoietin proteins demonstrated increased heat stability relative to the wild-type erythropoietin protein. Alterations in the noncoding regions of the erythropoietin gene can affect mRNA stability, rates of translation, expression from host cells, protein processing, export from rough **endoplasmic reticulum**, extend and pattern of glycosylation, **secretion** dynamics and rate of export from the cell. The free energy for mRNA secondary structure for nucleotides 401-624 in the 5'-**untranslated** region of the erythropoietin gene is predicted to be -161.0 kcal/mol, and deletions in this area decrease the free energy values; similar changes in free energy are obsd for nucleotides 2773-2972 in the 3'-**untranslated** region. Erythropoietin mutants with modified biol. activities may be of use to treat anemia.
SO PCT Int. Appl., 106 pp.
CODEN: PIXXD2

L10 ANSWER 3 OF 8 CAPLUS COPYRIGHT 2002 ACS
TI A signal recognition particle receptor gene from the early-diverging eukaryote, Giardia lamblia
AB The mol. mechanisms for targeting and translocation of **secreted** proteins are highly conserved from bacteria to mammalian cells, although the machinery is more complex in higher eukaryotes. To investigate protein transport in the early-diverging eukaryote, Giardia lamblia, we cloned the gene encoding the alpha subunit (SR.alpha.) of the signal recognition particle (SRP) receptor. SR.alpha. is a small GTPase that

functions in SRP-ribosome targeting to the ER. Sequence and phylogenetic analyses showed that SR.alpha. from G. lamblia is most homologous to SR.alpha. proteins from higher eukaryotes, although it lacks some conserved motifs. Specifically, giardial SR.alpha. has an N-terminal extension that enables SR.alpha. of higher eukaryotes to interact with a beta subunit that anchors it in the ER membrane. While the C-terminal regions are similar, giardial SR.alpha. lacks a prominent 13 amino acid regulatory loop that is characteristic of higher eukaryotic versions. Thus, giardial SR.alpha. resembles that of higher eukaryotes, but likely diverged before the advent of the regulatory loop. The 1.8 kb SR.alpha. transcript has extremely short **untranslated** regions (**UTRs**): a 1-2 nt 5'- and a 9 nt 3' **UTR** with the polyadenylation signal overlapping with the stop codon. RT-PCR, Northern and Western analyses showed that SR.alpha. is present at relatively const.
levels during vegetative growth and encystation, even though there are extensive changes in endomembrane structures and **secretory** activity during encystation. Immuno-EM showed that SR.alpha. localizes to
ER-like structures, strengthening the observation of a typical ER in G. lamblia. Unexpectedly, SR.alpha. was also found in the lysosome-like peripheral vacuoles, suggesting unusual protein traffic in this early eukaryote. Our results indicate that the eukaryotic type of cotranslational transport appeared early in the evolution of the eukaryotic cell.

SO Molecular and Biochemical Parasitology (**1999**), 98(2), 253-264
CODEN: MBIPDP; ISSN: 0166-6851

L10 ANSWER 4 OF 8 CAPLUS COPYRIGHT 2002 ACS

TI Cloning and characterization of the calreticulin gene from Ricinus communis L.

AB A full-length cDNA encoding a calreticulin-like protein was isolated by immune-screening a germinating castor bean endosperm cDNA library with antisera raised to the total lumenal fraction of purified plant **endoplasmic reticulum**. The calcium-binding properties of the recombinant protein were characterized and shown to be essentially identical to those reported for the mammalian calreticulin. Calcium overlays and immune blot anal. confirmed the endoplasmic lumenal identity of this reticuloplasmin. Probing protein blots of **endoplasmic reticulum** subfractions with radio-iodinated calreticulin showed specific assocns. with various polypeptides including one identified as the abundant reticuloplasmin protein disulfide isomerase. Characterization of the corresponding genomic clones revealed that calreticulin is encoded by a single gene of 3 kb in castor. The full genomic sequence reveals the presence of 12 introns, 12 translated exons, and one exon contg. the last three amino acids of the translated sequence and the 3'-**untranslated** region of the gene. Northern blot anal. of RNA isolated from various organ tissues showed a basal constitutive level of expression throughout the plant, but more abundant mRNA being detected in tissues active in **secretion**. This was confirmed in that anal. of transgenic tobacco plants contg. 1.8 kb of 5'-**untranslated** genomic sequence fused to the 3-glucuronidase reporter gene (GUS) showed a more localized pattern of expression. The chimeric gene was expressed in the vasculature (phloem, root hairs and root tip) in vegetative tissue, and was strongly expressed in the floral organs including the developing and germinating seed.

SO Plant Molecular Biology (**1997**), 34(6), 897-911
CODEN: PMBIDB; ISSN: 0167-4412

L10 ANSWER 5 OF 8 CAPLUS COPYRIGHT 2002 ACS

TI emo-1, a Caenorhabditis elegans Sec61p .gamma. homolog, is required for oocyte development and ovulation

AB Emo-1(oz1) is a member of a class of hermaphrodite sterile mutations in Caenorhabditis elegans that produce endomitotic oocytes in the gonad arm. Oocytes in emo-1(oz1) mutants exhibit multiple defects during oogenesis. After meiotic maturation, ovulation fails, trapping oocytes in the gonad arm where they become endomitotic. Emo-1 encodes a homolog of the Sec61p .gamma. subunit, a protein necessary for translocation of **secretory** and transmembrane proteins into the **endoplasmic reticulum** of yeast and mammalian cells. A putative emo-1 null mutation, oz151, displays embryonic lethality. The oz1 sterile mutation is a transposable element insertion into the emo01 3' **untranslated** region that almost completely eliminates germline mRNA accumulation. Genetic mosaic anal. using the oz1 allele indicates that emo01(+) expression in germ cells is required for fertility. The J67 monoclonal antibody, which recognizes an oocyte surface antigen does not stain oz1 oocytes, a finding consistent with defective protein transport in the mutant. The authors propose that the emo-1 gene product acts in the transport of **secreted** and transmembrane proteins in C. elegans oocytes, and is necessary for both oogenesis and the coupling of ovulation with meiotic maturation.

SO Journal of Cell Biology (**1996**), 134(3), 699-714
CODEN: JCLBA3; ISSN: 0021-9525

L10 ANSWER 6 OF 8 BIOSIS COPYRIGHT 2002 BIOLOGICAL ABSTRACTS INC.DUPLICATE 1

TI Characterization of a Phytophthora infestans gene involved in vesicle transport.

AB Members of the Ras superfamily of monomeric GTP-binding proteins have been shown to be essential in specific steps of vesicle transport and **secretion** in widely divergent organisms. We report here the characterization of a gene from Phytophthora infestans encoding a deduced amino acid (aa) sequence belonging to the Ypt class of monomeric GTP-binding proteins, products shown in other organisms to be essential for vesicle transport between the **endoplasmic reticulum** and the cis-Golgi compartments. Analysis of genomic and cDNA sequences of this gene, Piypt1, indicates that it contains five introns, one in the 5'-**untranslated** region. All introns are typical in beginning with GT and ending with AG. The region of the transcription start point displays a number of features characteristic of fungi and other eukaryotes, but it does not contain TATA or CAAT motifs. A single transcript is produced from the gene, which is polyadenylated, but the gene does not contain a recognizable polyadenylation signal. Genomic DNA blots indicate that Piypt1 is a single-copy gene. Comparisons of Ypt1 aa sequences indicate that P. infestans is more closely related to algae and higher plants than to the true fungi. The protein product of the Piypt1 gene, expressed in Escherichia coli, cross-reacts with antiserum against yeast Ypt1 protein and binds GTP. Furthermore, the Pivpt1 gene is able to functionally complement a mutant ypt1 gene in Saccharomyces cerevisiae. The aa sequence similarity, immunological cross-reactivity and functional attributes of Piypt1 make it likely that it is an authentic ypt1 gene which participates in vesicle transport in Phytophthora infestans.

SO Gene (Amsterdam), (1996) Vol. 181, No. 1-2, pp. 89-94.

ISSN: 0378-1119.

L10 ANSWER 7 OF 8 MEDLINE DUPLICATE 2
TI Characterization of the human gene that encodes the peptide core of **secretory** granule proteoglycans in promyelocytic leukemia HL-60 cells and analysis of the translated product.
AB Based upon the deduced amino acid sequence of a cDNA (cDNA-H4) that had been proposed to encode the peptide core of an eosinophil and a HL-60 cell **secretory** granule proteoglycan, a 16-amino acid peptide was synthesized. This peptide was then used to elicit rabbit antibodies for study of the translation and post-translational modification of this gene product in hematopoietic cells. When HL-60 cells were radiolabeled for 2 min with [35S]methionine, a protein that migrated in a sodium dodecyl sulfate-polyacrylamide electrophoresis gel with a Mr of 20,000 was immunoprecipitated with the IgG fraction of the anti-peptide serum. Kinetic experiments revealed that within 10 min this radiolabeled precursor protein was converted in HL-60 cells into an Mr approximately 150,000 chondroitin sulfate proteoglycan intermediate. After a 20-min to 1-h chase, this [35S]methionine- or [35S]sulfate-labeled proteoglycan intermediate lost its antigenicity, presumably due to proteolysis of its N terminus. A human genomic library was probed under conditions of high stringency with cDNA-H4 to isolate genomic clones that contain the gene that encodes this proteoglycan peptide core. This gene spans approximately 15 kilobases and consists of three exons. The first exon encodes the 5'-**untranslated** region of the mRNA transcript, as well as the entire 27-amino acid signal peptide of the translated molecule. The second exon encodes a 49-amino acid region of the peptide core, predicted to be the N terminus of the molecule after its proteolytic processing in the **endoplasmic reticulum**. The third exon encodes the remainder of the molecule, including its glycosaminoglycan attachment, serine-glycine repeat region. As assessed by S1 nuclease mapping and primer extension analysis, the transcription-initiation site in HL-60 cells for this gene resides 53 base pairs upstream from the translation-initiation site.
SO JOURNAL OF BIOLOGICAL CHEMISTRY, **(1990 Apr 5)** 265 (10) 5889-96. Journal code: 2985121R. ISSN: 0021-9258.

L10 ANSWER 8 OF 8 MEDLINE DUPLICATE 3
TI Cloning and characterization of the mouse gene that encodes the peptide core of **secretory** granule proteoglycans and expression of this gene in transfected rat-1 fibroblasts.
AB A mouse liver genomic library was probed with a 450-base pair AccI----3' gene-specific fragment of a mouse bone marrow-derived mast cell proteoglycan cDNA to isolate 15-18-kilobase (kb) genomic clones containing the gene that encodes the peptide core of mouse **secretory** granule proteoglycans. Based on the **nucleotide** sequences of its 2.0-3.5-kb subcloned fragments, this mouse gene consists of three exons. The first exon contains 41 base pairs of **untranslated** nucleotides that are present in the 5' region of the transcript and also encodes the hydrophobic 25-amino acid signal peptide. The second exon encodes a 48-amino acid sequence that would be predicted to be the N terminus of the peptide core after the signal peptide has been removed in the **endoplasmic reticulum**. The third exon encodes a 79-amino acid sequence that includes the 15 amino acids immediately preceding an alternating serine-glycine 21-amino acid sequence for glycosaminoglycan attachment, and the subsequent C-terminal 43 amino

acids; this exon also contains the 424 **untranslated** nucleotides present in the 3' region of the transcript. Primer extension and S1 nuclease protection analyses were performed to determine the transcription initiation site of the mouse gene. Rat-1 fibroblasts were cotransfected with the selectable marker pSV2 neo and a lambda clone (lambda MG-PG1) to obtain two rat-1 fibroblast cell lines that had the mouse **secretory** granule proteoglycan gene integrated into their genomes. RNA blot analysis of both cell lines revealed the presence of the 1.0-kb **secretory** granule proteoglycan peptide core mRNA transcript, indicating that lambda MG-PG1 contained the entire mouse **secretory** granule proteoglycan peptide core gene including some of the regulatory elements in its promoter region. The gene that encodes the peptide core of mouse **secretory** granule proteoglycans is the first proteoglycan gene to have its complete exon/intron organization determined and to be transfected and expressed in another cell type.

SO JOURNAL OF BIOLOGICAL CHEMISTRY, **(1989 Oct 5)** 264 (28) 16719-26. Journal code: 2985121R. ISSN: 0021-9258.

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FILE 'MEDLINE, BIOSIS, CAPLUS' ENTERED AT 16:20:41 ON 11 OCT 2002

L1	39186	UNTRANSLATED OR UTR
L2	326505	NUCLEIC ACID
L3	741097	?NUCLEOTIDE
L4	992685	L2 OR L3
L5	20263	L1 AND L4
L6	107392	ENDOPLASMIC RETICULUM
L7	94	L5 AND L6
L8	16	L7 AND SECRET?
L9	13	L8 AND 1970-2000/PY
L10	8	DUP REM L9 (5 DUPLICATES REMOVED)

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